

RISK OF LUNG CANCER AND RESIDENTIAL RADON IN CHINA: POOLED RESULTS OF TWO STUDIES

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Studies of radon-exposed underground miners predict that residential radon is the second leading cause of lung cancer mortality; however, case-control studies of residential radon have not provided unambiguous evidence of an association. Owing to small expected risks from residential radon and uncertainties in dosimetry, large studies or pooling of multiple studies are needed to fully evaluate effects. We pooled data from 2 case-control studies of residential radon representing 2 large radon studies conducted in China. The studies included 1,050 lung cancer cases and 1,996 controls. In the pooled data, odds ratios (OR) increased significantly with greater radon concentration. Based on a linear model, the OR with 95% confidence intervals (CI) at 100 Becquerel/cubic-meter (Bq/m³) was 1.33 (1.01,1.36). For subjects resident in the current home for 30 years or more, the OR at 100 Bq/m³ was 1.32 (1.07,1.91). Results across studies were consistent with homogeneity. Estimates of ORs were similar to extrapolations from miner data and consistent with published residential radon studies in North American and Europe, suggesting long-term radon exposure at concentrations found in many homes increases lung cancer risk.

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Studies of underground miners demonstrate that inhalation of high levels of radioactive radon gas (more precisely ²²²Rn) increases risk of lung cancer.¹ The ubiquitous presence of radon in homes, although at concentrations generally below those in mines, raises concern about the contribution of radon to lung cancer risk in the general population. Extrapolations using miner-based models suggest radon may be the second leading cause of lung cancer, which may, for example, be responsible for 7% of lung cancers in Germany,² 4% in the Netherlands,³ 20% in Sweden,³ 11% in Norway⁴ and 10–15% in the United States.^{1,5} To assess validity of these estimates, investigators have conducted epidemiological studies of residential radon and lung cancer in many countries.

There are inherent difficulties in identifying excess lung cancer risks from residential radon. The expected risk is small and radon dosimetry has substantial uncertainty due to the need to characterize exposures many years prior to lung cancer diagnosis.^{6,7} Uncertainties are linked to use of current radon measurements in rooms as indicators of past concentrations, to adjustment for structural and other modifications of homes over time, and to accounting for population mobility since current residents of prior homes of study subjects may have different lifestyle patterns that alter concentrations. Consequently, large numbers of subjects with accurate exposure assessment are needed.

Meta-analyses of published results and pooling of original data from multiple studies offer approaches for addressing sample size limitations. While epidemiologic studies of residential radon and lung cancer have seemingly produced equivocal evidence of an increased risk, meta-analyses have found statistically significant excess risks from residential radon.^{8,9} Cooperative workshops to guide pooling of studies have been underway.^{10–13} The first of these efforts, the pooling of 7 North American radon studies, was

recently been completed¹⁴ and showed increased risks with radon exposure.

There have been 2 case-control studies of lung cancer and indoor radon conducted in China, 1 study in Shenyang an urban area in northeastern China^{15,16} and 1 study in eastern Gansu province,¹⁷ which used 1-year radon detectors and personal interviews to obtain data on smoking and other risk factors. The current report pools the data from these 2 studies.

MATERIAL AND METHODS

Following recent practice^{14,18} we assume the disease-relevant exposure time window (ETW) is 5–30 years prior to disease incidence for cases or interview for controls and assess exposure within this period. Analysis of miners indicates that exposures 5 to 30 years prior to lung cancer have the greatest impact on risk.¹

Shenyang case-control study

The Shenyang study included all incident lung cancer cases recorded with the Shenyang Cancer Registry and diagnosed between September 1985 and September 1987.^{15,16} Nearly all cases were interviewed within 1 month of diagnosis. Five percent of cases who were too ill for interview or had died were excluded. An expert panel of pulmonary disease physicians and pathologists reviewed all diagnostic material. Controls were randomly sampled from the general population and matched on sex and age to cases. A total of 520 female and 729 male cases and 557 female and 788 male controls were interviewed.

The radon component of the study enrolled females only and did not begin for 6 months, so that not all females were included in the radon component. Radon measurements were obtained from 78% (308 of 397) and 91% (356 of 391) of eligible cases and controls, respectively. For the current analysis, we were able to retrieve data on 301 cases and 355 controls. We searched documentation and computer files but were unable to determine the reason for the loss of the 8 subjects.

Radon was measured in 1 home for each subject. Alpha-track detectors were placed for 1 year in the current home, if the subject had resided there at least 5 years. If that criterion was not met, detectors were placed in the previous residence, provided it was located in Shenyang, accessible and the subject lived there for 5 years or more. Subjects resided in the measured home for a median of 24 years. Two detectors were placed in each home, 1 in the

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bedroom and 1 in the living room. Two measurements were obtained for 95% of subjects. The mean of both measurements, when available, was used in analysis, otherwise the single measurement was used. We omitted 2 subjects (controls) with extreme radon values (1,219 and 1,659 Bq/m³) that were more than 50% greater than the next largest value and 4 standard deviations from the mean.

Original analyses did not characterize radon within an ETW. For this pooling, we calculated time-weighted average (TWA) radon concentration for the 5–30 year ETW. This resulted in the deletion of 16 cases (mean 91.9 Bq/m³) and 13 controls (mean 61.6 Bq/m³) who resided in their measured homes for precisely 5 years prior to enrollment, and therefore had no measurements within the ETW. Thus, 95% of cases (285 of 301) and 95% of controls (338 of 355) remained. For unmeasured years within the ETW, we inserted the mean radon concentration of control homes when calculating TWA radon concentration, an approach that is approximately unbiased with rare diseases and data missing at random.¹⁹

Gansu case-control study

The Gansu study included all incident cases of lung cancer occurring in 2 rural prefectures of Gansu Province between June 1994 and April 1998.¹⁷ A substantial proportion of the population lived in a unique style of underground dwellings where concentrations of radon are high.²⁰ Study personnel identified cases by visiting all relevant medical facilities. An expert panel of pathologist, radiologists and clinicians from the Gansu Department of Health reviewed all diagnostic material. Investigators enrolled 886 lung cancer cases (656 males and 230 females). Because half of the cases, although incident, were identified retrospectively, 464 (52.4%) cases were deceased and next-of-kin were interviewed. Controls were randomly selected from 1990 population census lists and matched by age in 1995, sex and prefecture to an expected distribution of case ages, which was determined from a review of 1991 medical records. There were 1,765 (455 females and 1,310 males) control subjects. Next-of-kin were interviewed for 71 (4.0%) deceased controls.

For each subject, 2 alpha-track detectors (1 in the living room and 1 in the bedroom) were placed for 1 year in each home occupied for 2 or more years during the 30 years prior to the enrollment date and located within the 2 prefectures. Eighty-eight percent (775 of 881) of cases and 95% (1,669 of 1,765) of controls had at least 1 measurement within the 5–30 year ETW period.

We used mean radon concentrations for control homes within prefecture and construction style to impute concentrations for unmeasured time periods.¹⁹

Statistical analysis

We computed odds ratios (OR) and 95% confidence limits (CI) using standard logistic regression. For the Shenyang data, we adjusted analyses for age and an index of air pollution (defined in reference 16), categorized by tertiles. For the Gansu data, we adjusted for age, prefecture of residence, sex and socioeconomic factors, which were characterized by ownership of a color television (2 levels) and number of large domestic animals (3 levels; 0, 1, ≥ 2).¹⁷ Age categories were common across studies (7 levels: <45, 45–49, 50–54, 55–59, 60–64, 65–69 and ≥ 70 years). We adjusted both studies by a smoking risk variable (4 levels: ≥ 40 years smoking ≥ 20 cigarettes equivalents per day; ≥ 30 years smoking ≥ 10 cigarettes equivalents per day; other smokers and never-smokers) with subjects assigned their highest risk category. Pooled ORs were further adjusted for study. After excluding subjects with missing data, there were 275 cases and 333 controls from Shenyang, and 753 cases and 1,641 controls from Gansu.

We fit a linear excess odds ratio (EOR) model, $OR = 1 + \beta x$, where x is TWA radon concentration and β is the EOR per Becquerel per cubic-meter (Bq/m³), and computed likelihood-based 95% confidence intervals (CI). We evaluated variation of radon effects across other factors (effect modification) by fitting

category-specific EORs, $1 + \beta_j x_j$, where x_j is radon concentration and β_j is the EOR/Bq/m³ within level j , using a likelihood ratio test.

Preliminary analysis indicated that coverage of the ETW and residential mobility may be confounding variables. In Gansu controls, radon levels were higher in subjects with less than complete coverage and higher in subjects with higher mobility. In Shenyang controls, radon was uncorrelated with coverage but positively correlated with number of residences. We additionally adjusted EOR models for mobility within the ETW (1, 2, ≥ 3 homes) and coverage (<20, 20–24, ≥ 25 years).

Study-specific results differ slightly from previously published results due to different categorizations for adjustment factors.

RESULTS

For Shenyang subjects, cases and controls had similar ages at enrollment, and exposure to indoor pollution (Table I). For Gansu subjects, cases were younger, more likely deceased, owned a color television and had fewer large domestic animals. Age differences in the Gansu study were due to the selection of controls based on ages in 1995 and an extension of the case enrollment period. Age differences did not effect results since analyses adjusted for age at enrollment.

In Gansu controls, nearly all males (91.0%) smoked, while nearly all females (90.2%) did not, and in Shenyang controls 36.8% of females smoked (Table II). Among smokers, tobacco consumption was generally light. Means for number of cigarettes smoked per day and duration of use were 10.7/days and 30.2 years for Gansu males, 5.4/days and 22.1 years for Gansu females, and 17.3/day and 34.7 years for Shenyang females. ORs increased with increasing tobacco use in Shenyang females and Gansu males.

Shenyang females tended to be more mobile than subjects from the more rural Gansu study areas. Within the 5–30 year ETW, Shenyang females on average lived in 2.0 residences, with 1 measured per subject, while Gansu subjects resided in 1.7 residences for both females and males, with 1.2 residences measured per subject. Radon measurements covered 67.2% and 67.7% of the ETW for cases and controls in Shenyang, respectively, and 71.8% and 79.1% of the ETW for Gansu cases and controls. The arithmetic mean (AM), geometric mean (GM) and geometric standard deviation (GSD) for radon were 115.7, 91.2 and 1.93 Bq/m³ for Shenyang detectors, respectively, and 222.9, 176.2, and 2.08 Bq/m³ for Gansu detectors. Measurements exceeded 150 Bq/m³ for 17.4% of Shenyang homes and 65.7% of Gansu homes. AMs for TWA radon concentrations for cases and controls were 122.1 and 122.7 Bq/m³ for Shenyang, respectively, and 232.3 and 225.7 Bq/m³ for Gansu.

ORs for lung cancer generally increased with radon concentration in Gansu, while ORs for Shenyang subjects were generally near 1 and did not exhibit a trend (Table III).

For the pooled data, the EOR at 100 Bq/m³ and 95% CI were 0.133(0.01,0.36) (Table IV). The EOR was significant for the Gansu data, 0.175 (0.02,0.49), but not for the Shenyang data, -0.019 ($-0.13,0.43$), although homogeneity of EORs was not rejected ($p=0.29$). Figure 1a shows ORs plotted at category means and the pooled linear OR model.

Table IV also shows EORs by coverage and number of homes in the ETW. For Shenyang, EOR was increased, but not significantly, in subjects with complete coverage (or resident in 1 home in the ETW), 0.177 ($-0.12,2.04$). For subjects with less than 20 years coverage or resident in 3 or more homes, EORs were 0.330 ($-0.16,\infty$) or 0.431 ($-0.17,\infty$), respectively. The latter 2 estimates were unstable due to the narrow range of exposures, since mean coverage of the ETW was less than 9 years, implying that a single imputed mean value was used for 16 years in the TWA radon calculation. For Gansu, EORs were significantly elevated only for subjects with complete coverage, 0.355 (0.09,1.08), or resident in

TABLE I—NUMBERS OF LUNG CANCER CASES AND CONTROLS, AND DEMOGRAPHIC INFORMATION FOR STUDIES IN CHINA

	Shenyang ¹		Gansu			
	Females		Females		Males	
	Cases	Controls	Cases	Controls	Cases	Controls
Total subjects	285	338	205	427	563	1,232
Age at enrollment (y)	56.2	56.7	53.7	55.3	55.8	56.6 ²
Age at enrollment (%)						
<45	7.3	6.8	17.1	11.5	13.3	11.5
45–49	7.6	7.4	17.6	16.4	8.2	15.3
50–54	20.3	19.7	18.5	20.4	20.6	14.7
55–59	31.6	27.4	14.6	17.1	19.2	16.5
60–64	22.6	23.6	17.6	15.5	21.5	17.9
65–69	10.6	15.1	10.7	12.4	11.7	21.5
70+			3.9	6.8	5.5	5.5 ²
Ownership of color TV (%)			31.7	17.3 ²	33.4	19.0 ²
Number of large domestic animals (%)						
0			24.9	32.3	22.7	30.2
1			22.4	33.5	28.9	30.9
≥2			52.7	34.2 ²	48.3	38.9 ²
Indoor air pollution index (%) ³						
I	34.9	36.9				
II	21.1	20.7				
III	44.0	42.3				
Type of respondent (%)						
Subject	100.0	100.0	48.8	97.0	48.3	95.5
Proxy	0.0	0.0	51.2	3.0 ²	51.7	4.5 ²

¹Includes only subjects with measurement data within the 5–30 year exposure time window (ETW).—² $p < 0.01$ for test of homogeneity of distributions in cases and controls.—³Categories based on tertiles in controls.

TABLE II—NUMBERS OF SUBJECTS, ODDS RATIOS (OR) FOR LUNG CANCER AND A SMOKING RISK VARIABLE FOR THE SHENYANG AND GANSU CHINA RESIDENTIAL RADON STUDIES¹

	Shenyang			Gansu						Pooled studies		
	Cases	Controls	OR	Females			Males			OR	95% CI	p ²
				Cases	Controls	OR	Cases	Controls	OR			
Never smoked	113	213	1.00 ³	181	385	1.00 ³	28	110	1.00 ³	1.00 ³		
Ever smoked	162	120	2.95	23	42	1.14	521	1,104	1.98	2.28	(1.8,3.0)	0.04
Smoking risk ⁴												
I	54	61	1.79	20	36	1.30	310	749	1.73	1.77	(1.3,2.3)	
II	75	42	4.00	3	6	0.61	171	314	2.61	2.93	(2.2,4.0)	
III	33	17	5.54 ⁵	0	0	—	40	41	3.85 ⁵	4.47 ⁵	(2.8,7.1)	0.32

¹ORs adjusted for age, sex (both studies), air pollution index (Shenyang), prefecture and socioeconomic factors (Gansu). Pooled ORs additional adjusted for study.—² P -value for test of homogeneity across studies.—³Reference category for ORs.—⁴Variable defined as III, 40 or more years smoking 20 or more cigarettes equivalents per day; II, 30 or more years smoking 10 or more cigarettes equivalents per day; I, other smokers, with subjects assigned their highest risk category.—⁵ $P < 0.001$ for test for trend in ORs.

1 home in the ETW, 0.372 (0.08,1.28). In the pooled data, EORs varied significantly by coverage and number of homes. EORs were 0.319 (0.09,0.88) with complete coverage and 0.332 (0.08,0.96) for subjects resident in 1 home. EOR patterns were homogeneous across studies.

The most accurate dosimetry likely occurs for subjects with complete coverage and 1 home in the ETW. Restricting data to these subjects and for radon categories <100, 100–149, 150–199, 200–249, 250–299, ≥300 Bq/m³, ORs and 95% CIs were 1.00, 1.50 (0.8,2.9), 1.21 (0.3,5.2), 2.43 (0.6,10.0) and 1.39 (0.5,4.5) (the upper 2 categories were merged due to few subjects), respectively, for Shenyang, and 1.00, 0.99 (0.6,1.8), 1.34 (0.8,2.4), 1.37 (0.8,2.4), 0.89 (0.46,1.74) and 1.91 (1.1,3.3) for Gansu. For the pooled data, ORs and 95% CIs were 1.00, 1.18 (0.8,1.8), 1.44 (0.9,2.3), 1.53 (0.9,2.5), 1.05 (0.6,1.9) and 1.93 (1.2,3.1), with an EOR of 0.315 (0.07,0.91). Figure 1b shows ORs and the EOR estimate for the restricted data.

We evaluated EORs for radon by categories of sex, indoor smokiness and cigarette smoking variables for all subjects and for subjects with complete coverage and resident in 1 home in the ETW, and found no significant variation. EORs differed significantly only for type of respondent, with EORs at 100 Bq/m³ of 0.086 and –0.090 ($p=0.01$) for subject and surrogate respondent,

respectively, and 0.382 and –0.096 ($p=0.01$) among subjects with complete coverage.

DISCUSSION

The pooling of 2 Chinese radon studies showed an excess risk of lung cancer with increased residential radon concentration. Restrictions on the data suggestive of improved exposure assessment increased estimates of excess risk. The EORs at 100 Bq/m³ were 0.133 (0.01,0.36) in the complete data and increased to 0.315 (0.07,0.91) in subjects with complete coverage and resident in 1 home within the ETW. These EORs were similar to estimates in a pooling of North American radon studies, 0.106 (0.00,0.28) for subjects with dosimetry based on long-term detectors and 0.205 (0.03,0.50) for subjects with complete coverage.¹⁴ EORs were similar to the extrapolation from miner data, which estimates an EOR at 100 Bq/m³ of 0.117.¹

Variations of the EORs with other factors were similar to results in the North American pooling.¹⁴ Both analyses found similar EORs for never-smokers and ever-smokers, and no significant variation of effects of attained age. These patterns differed from those in miner studies, where exposure-response trends were significantly lower among ever-smokers and at older ages at diagno-

TABLE III – ODDS RATIO (OR) OF LUNG CANCER BY TIME WEIGHTED AVERAGE RADON CONCENTRATION WITHIN THE 5–30 YEAR EXPOSURE TIME WINDOW (ETW) PRIOR TO ENROLLMENT¹

	Radon concentration, Bq/m ³						Total
	<100	100–149	150–199	200–249	250–299	≥300	
<i>Shenyang study</i>							
Cases	101	138	14	10	3	9	275
Controls	131	152	20	15	4	11	333
Mean	70.9	121.5	173.1	218.4	272.3	475.0	122.4
OR	1.00 ²	1.29	1.16	0.75	1.06	1.05	
95% CI		(0.8,2.0)	(0.5,2.7)	(0.3,2.0)	(0.2,5.8)	(0.4,3.0)	
<i>Gansu study</i>							
Cases	63	85	184	171	111	139	753
Controls	167	235	334	357	252	296	1,641
Mean	69.5	128.4	177.4	223.0	274.5	411.3	227.8
OR	1.00 ²	1.00	1.46	1.17	1.28	1.56	
95% CI		(0.6,1.6)	(0.9,2.3)	(0.7,1.8)	(0.8,2.1)	(1.0,2.5)	
<i>Pooled studies</i>							
OR	1.00 ²	1.12	1.42	1.13	1.27	1.52	
95% CI		(0.8,1.5)	(1.0,2.0)	(0.8,1.6)	(0.8,1.9)	(1.1,2.2)	

¹ORs adjusted for age, sex, smoking risk, years in ETW, number of homes (both studies), an indoor pollution index (Shenyang), prefecture and socioeconomic factors (Gansu). Pooled model adjusted for study.– ²Referent category for ORs.

TABLE IV – EXCESS ODDS RATIO (EOR) FOR RADON CONCENTRATION OVERALL AND BY YEARS COVERED BY RADON DETECTORS AND RESIDENTIAL MOBILITY WITHIN THE 5–30 YEAR EXPOSURE TIME WINDOW (ETW) PRIOR TO ENROLLMENT¹

Model for EOR	Pooled studies			Shenyang			Gansu			<i>p</i> ⁴
	$\beta \times 100$	Deviance ²	Cases	$\beta \times 100$	Deviance ²	Cases	$\beta \times 100$	Deviance ²	Parameters ³	
Overall (95% CI)	0.133 (0.01,0.36)	—		−0.019 (−0.13,0.43)	—		0.175 (0.02,0.49)	—	1	0.29
Years in ETW										
25	0.319		106	0.177		358	0.355			
20–24	−0.134		39	−0.134		74	−0.097			
<20	−0.072	10.21 ⁵	130	0.330	3.95	321	−0.128	7.08 ⁵	3	0.58
Homes										
1	0.332		106	0.173		243	0.372			
2	−0.071		100	−0.134		362	−0.029			
≥3	0.099	6.39 ⁵	69	0.431	3.36	148	0.031	3.96	3	0.56

¹Based on the linear odds ratio model: $OR(x) = 1 + \beta x$, where x is the mean radon concentration within ETW. Models adjusted for age, sex, smoking risk, years in ETW, number of homes (both studies), an indoor pollution index (Shenyang), prefecture and socioeconomic factors (Gansu). Pooled model adjusted for study.– ²Change in deviance relative to overall model.– ³Number of parameters used to model EOR.– ⁴*P*-value for test of homogeneity of EOR parameters across studies.– ⁵Test of homogeneity (change in deviance) relative to overall model without effect modifiers statistically significant, $p < 0.05$.

sis.¹ The reasons for these differences have not been explored but may relate to the higher exposures in miners, cessation at retirement of exposure to occupational lung cancer risk factors and lung irritants, such as arsenic and silica dusts, or incomplete control of the effects of cessation of radon exposure or of tobacco consumption.

The EOR for radon was nearly identical for males and females in the Chinese and North American pooled analyses. This result has important implications for radon risk assessment in the general population. The current practice for estimating attributable risk for lung cancer from residential radon assumes exposure to radon multiplies the background lung cancer rates by the same factor for males and females, and applies the miner-based risk model to males and to females. This contrasts with an assumption of an additive translation of radon effects, where the excess lung cancer risk from radon in males is added to the background lung cancer risk in females.^{21,22} The pooled analyses provide empirical evidence supporting the proportionality assumption and a similar attributable risk from radon for both sexes.

A positive EOR was observed for subject respondents but not for next-of-kin respondents. Radon is a physical measurement, and the placement and reading of the radon detectors are not likely influenced by vital status. Differences by type of respondent may be related to accuracy of the information used for adjustment and for residential histories, with greater uncertainty from next-of-kin respondents perhaps resulting in a bias towards the null in that

subgroup. This variation was again similar to the findings in the North American pooling.

The Gansu study included nearly 3 times the number of lung cancer cases and had higher mean exposures than the Shenyang study, and thus played a dominant role in the pooled results. However, use of original data allowed parallel, as well as pooled, analysis under consistent definitions of variables and with application of a consistent methodology, in contrast to meta-analysis of published results. As in the original analysis of the Shenyang data,¹⁶ we found no overall association of radon exposure and risk of lung cancer. We did find however positive, albeit not significant, risk patterns with radon exposure, particularly in restricted subsets of the data. In the current analysis, dosimetry was based on a 5–30 year ETW with the mean of control detectors used to impute gaps, while the original dosimetry used only measured radon without imputing unknown values and without accounting for duration of residency. For a (relatively) rare disease such as lung cancer and assuming that missingness is noninformative, the imputation approach we applied is unbiased.¹⁹ The original dosimetry was equivalent to assigning an individual's observed radon to unmeasured homes within the ETW, whereas our analysis imputed population mean values. The former approach may have increased error by using a single value to estimate radon in the entire ETW and may bias results towards the null.^{23,24}

In contrast to the Gansu data, mean coverage of the ETW for the Shenyang subjects was the same in cases and controls; however,

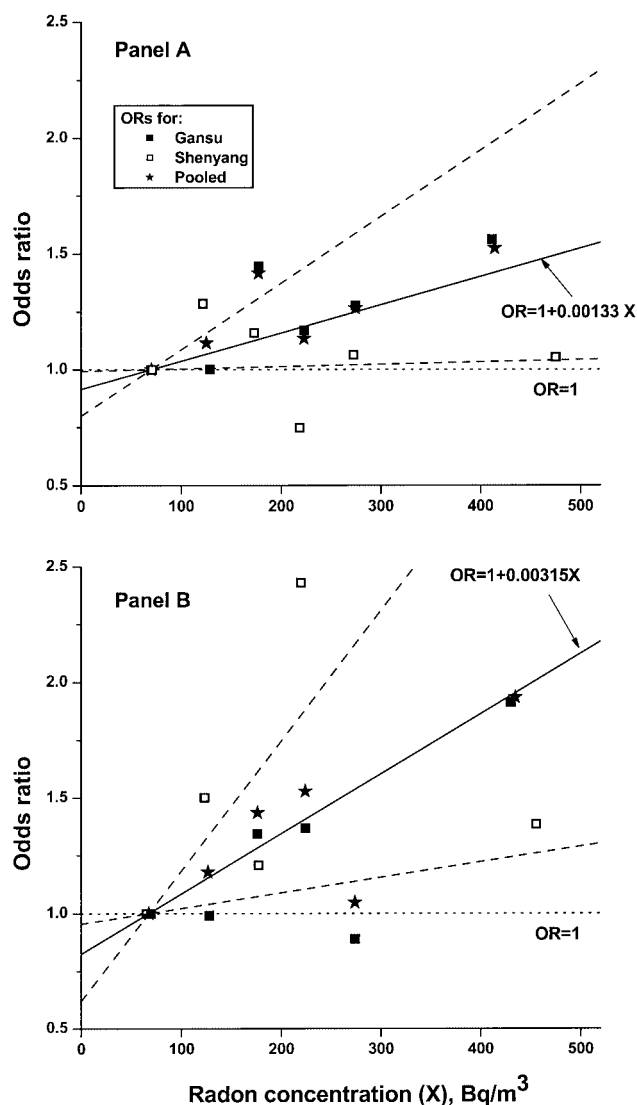


FIGURE 1 – Odds ratios (OR) of lung cancer for categories of radon concentration for the Shenyang and Gansu case-control data, and ORs and the fitted linear odds ratio model (solid line) and 95% confidence limits (dashed lines) for the pooled data. Results shown for all subjects (a) and for subjects with complete coverage of the 5–30 year exposure time window and resident in 1 home (b). Each OR is plotted at its category-specific mean concentration.

coverage was positively correlated with radon levels in cases and nearly uncorrelated in controls. Consequently, in controls, deriving ETW-based exposures from original measurements uniformly adjusted values across all coverages independent of concentrations. In cases, subjects with lower coverage were more likely to also have lower radon levels and so were differentially influenced by the imputation in ETW calculations. Original analyses did not account for potential confounding due to coverage since there was no *a priori* reason to posit that coverage was related to both radon exposure and disease risk.

We deleted 2 Shenyang controls whose radon measurements were more than 50% greater than the next largest value and more than 4 standard deviations from the mean, although there was no indication values were invalid, except for their extremity. The subjects were influential. For the Shenyang data, the EORs changed from -0.019 to -0.060 with the 2 extreme concentrations included. For subjects with complete coverage of the ETW, EORs changed from 0.177 to 0.020 when the outliers were included. It is noteworthy that if we excluded 20 subjects with concentrations of 300 Bq/m^3 or above (the highest category of Table IV) or 14 subjects in the restricted data, EORs were -0.010 overall and 0.935 in the restricted data. Inclusion of the 2 extreme Shenyang exposures reduced the pooled estimate from 0.133 ($0.01, 0.36$) with $p=0.29$ for the test of homogeneity to 0.102 ($-0.01, 0.31$) with $p=0.05$ for the test of homogeneity overall, and from 0.315 ($0.07, 0.91$) with $p=0.60$ for the test of homogeneity to 0.278 ($0.06, 0.82$) with $p=0.27$ for the test of homogeneity in subjects with complete coverage and 1 residence.

Uncertainties in radon dosimetry limit precise estimation of risk in residential studies. Uncertainties arise from use of current measurements of radon in air to reflect past levels, which may differ due to changes in living patterns, structural alterations or normal yearly random variation. Uncertainty is also increased due to imputation of concentrations for gaps in the ETW, homes that no longer exist, homes located outside the study area, homes occupied briefly and not measured or the owner's refusal to allow measurements.^{6,7,23,24} Time or movement within the home may be ignored or inadequately characterized.^{25–27} Investigators have addressed uncertainties by explicitly adjusting risk estimates under various probability models,^{23,24,28–30} conducting sensitivity analyses,³¹ limiting study participants to long-term residents^{26,32} or using improved dosimeters.^{33–35} Analyses have suggested that accounting for uncertainties may increase estimates of EORs 50–100%.^{23,24,28,29,31} A similar impact of uncertainties was reported for the Gansu study, based on modeling temporal and spatial variability in radon levels using data from a 3-year study of 55 houses.³⁰

In summary, the estimates of the EOR from 2 different areas of China, 1 rural and 1 urban, were consistent with homogeneity and were similar to summary estimates from studies in North America and Europe and to extrapolations from miners. These analyses provide additional evidence that residential radon increases lung cancer risk in the general population.

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